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VA Research Currents

'The present of a few years'

By John R. Feussner, MD, MPH, Chief R&D Officer

Editor's note: Dr. Feussner, who has served in his current position since 1996 and has conducted research for VA for 28 years, is retiring from the department as of Aug. 16 to become Chairman of Medicine at the Medical University of South Carolina. This is his farewell column for readers of VA Research Currents.

During my presentations to the veterans service organizations (VSOs), I reminded them of the promise of biomedical research by quoting a phrase from Sir William Osler: "Modern science has made to almost every one of you the present of a few years."

Amid the stress of the daily effort to care for the burgeoning medical needs of sick veterans and the persistent challenge of budget shortfalls, it is easy to focus on the problems of today and to see the future as someone else's challenge. After all, how can we worry about tomorrow when we cannot be certain about today? Therein lay the conundrum challenging all medical researchers: Not only must you do the best research, but you must also make that work useful to our patients. You must also better communicate the promise of biomedical research to leaders and policy makers who set the department's agendas. No one can perform that task better than the researchers themselves.

I challenge you to become a better ombudsman for the biomedical research enterprise. Do not leave this key task to others because you are too busy, over-stressed, underappreciated, or adequately funded for another period of time. Please continue to communicate, cajole, convince, even *confront* our leadership with the enduring need for medical research and the precious time to accomplish research tasks.

The biomedical scientists will continue to acquire new understanding and knowledge about the basic mechanisms of disease, and with that new understanding will create innovations to help our patients. The clinical trialists will

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Input sought for planning national VA biorepository

If you have experience collecting and storing human biological samples, Louis Fiore, MD, wants to talk to you.

Fiore, of the Cooperative Studies Program (CSP) Massachusetts VA Epidemiology Research and Information Center (MAVERIC) in Boston, is at the helm of an effort to create a national VA biorepository to store human tissue samples—and manage the related clinical data—for future use by VA researchers. He said his group is eager to tap into expertise within VA. "We don't want to overlook VA

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VA study: Common knee surgery no better than placebo

Patients with osteoarthritis of the knee who underwent mock arthroscopic surgery were just as likely to report pain relief as those who received the real procedure, according to a VA-funded study published in the July 11 *New England Journal of Medicine.* The results challenge the usefulness of a common medical procedure on which Americans spend more than $3 billion each year.

"If the effectiveness of arthroscopic lavage or debridement in patients with osteoarthritis of the knee is no greater than that of placebo surgery, the billions of dollars spent each year on these procedures might be put to better use," said lead investigator Nelda P. Wray, MD, MPH, a health services researcher at the Houston VA Medical Center and Baylor College of Medicine.

In the study, 180 patients with knee pain were randomized into three groups. One group received debridement, in which worn, torn or loose cartilage is cut away and removed with the aid of a pencil-thin viewing tube called an arthroscope. The second group underwent arthroscopic lavage, where the bad cartilage is flushed out. The third group underwent a procedure with only the appearance of

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'The present of a few years' (cont. from page 1)

continue to evaluate new treatments for effectiveness, safety and cost. The health services researchers, through QUERI and other initiatives, will continue to translate current knowledge into improved systems performance and enhanced quality of lives for our veteran patients. And rehabilitation scientists and engineers will pursue future cures, but also conduct research to restore independence for disabled patients today.

We have often asserted that our veteran patients have served our country twice—first, in our nation's defense against external enemies, and now, as volunteers in our research, often for purely altruistic reasons. But many of our VA researchers also serve our veteran patients twice: As the large majority of our researchers are clinicians, they do more than explore the cutting edge of science to improve the future health care for veterans. As physicians, nurses, and other clinical caregivers, they also provide for our patients' health needs today. What a powerful combination, these veterans and these medical researchers–both doing double duty in their respective ways, dedicated to their country, to their fellow citizens, to a better tomorrow.

I have been privileged to work with both groups extensively over the past few years. I am ever grateful for that opportunity. Our veteran patients, and their national representatives in the VSOs, have never hesitated in their support of our research. They really do get it!

And to you, our researchers, who continue to struggle with too little funding, too little time, too little research space and equipment, and too often, too little understanding from their leaders—I encourage you to persist with your determined efforts. Our patients deserve your best work.

I will miss your brilliant, dedicated, and tenacious efforts. I have no doubt you will produce future discoveries that lead to better health care for veterans. And I will be there, if only in spirit, to celebrate your achievements yet to come. But you too deserve our best efforts from medical center directors, VISN managers, and leaders here in Washington. Over these past few years, I have given you my best effort. In some ways, I am sad to leave. I believe that many challenges have not been addressed completely. I regret that I was unable to do more, better, or faster. But I do cherish what we shared together, *"the present of a few years."* Thank you all, my friends and colleagues. ■

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arthroscopic surgery; small incisions were made, but no instruments were inserted and no bad cartilage removed.

During two years of follow-up, all the patients reported modest improvements in pain and the ability to walk and climb stairs, with no significant differences among the three groups. In

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Do media report on studies prematurely?

A quarter of the studies presented at scientific meetings and reported on by the media never make it into peer-reviewed journals, according to research by a team at the White River Junction (Vt.) VA Medical Center. Their report appeared in the June 5 *Journal of the American Medical Association.*

Research results presented at scientific meetings are often preliminary, and have not yet undergone the rigorous, extensive review required for publication in the scientific literature. Yet these findings are frequently reported to the public.

Lisa Schwartz, MD, and Steven Woloshin, MD, searched news coverage following five major scientific meetings in 1998, and found stories on 147 abstracts. They then searched Medline and contacted the authors of those abstracts to see if their research had been published in the medical literature within three years or so after the meetings. Of the studies that had been reported on in newspapers, 25 percent remained unpublished in the literature. The rate of publication was the same for abstracts that had received front-page coverage.

Abstracts promoted to the media through press releases from meeting organizers were somewhat more likely to gain front-page coverage.

Schwartz and Woloshin suggest that abstracts may need to be more rigorously reviewed before being presented at meetings and communicated to the media.

Schwartz is a Health Services Research and Development Career Development awardee. ■

Plans under way for national VA biorepository (cont. from page 1)

investigators who are already out there doing this," said Fiore. "We invite them to help us move forward with proposing and building a VA system." He added that opportunities may also exist for a VA pathology department to participate as a processing center for tissue preparation and related tasks.

The first stage of the plan, the so-called "Legacy Survey," is winding down. As of July 15, all VA research sites were required to have answered a survey on their existing tissue-banking resources. Part of the impetus for the survey was to make sure investigators are strictly complying with regulations.

"We're trying to educate the bank owners, or principal investigators, as to what the standards are," said Fiore. "We want to make sure, for their own protection, that they have in place standard operating procedures, and plans to ensure appropriate IRB [institutional review board] approval to continue their research. Most of the existing resources were initially created prior to the current regulations."

Responses to Legacy Survey reveal wide range of archived samples

So far, survey responses reveal a wide range of human samples, collected by VA investigators for a variety of research purposes: DNA, blood, breast milk, cancer cells, saliva, urine, brains, livers, and other tissues. Once all the legacy data is collected, plans will move forward to build a tissue-banking program from the ground up.

"We think the value is in collecting tissue prospectively, because you can then ensure the quality of the tissue, and you can make sure the clinical data you need is available—that it hasn't been lost because the patients were seen five or 10 years ago," Fiore said.

Approved individual tissue banks at VA medical centers may have the option to continue storing their own samples, independent of the main biorepository. But according to MAVERIC's David Rose, MD, MPH, who is coordinating the Legacy Survey with Fiore, the national facility will not only ensure high quality storage and data management, but effectively promote and distribute available samples to interested researchers for the benefit of science. He points out that contributing investigators would help define how their tissues would eventually be used.

"If investigators decide to involve their tissue in our distribution network, then we could all leverage our resources," said Rose. "A lot of the sample sets that have been collected aren't promoted right now. Some physicians are finding they don't have the time for it. And that's just what we're going to be dedicated to doing. So in some cases it might make sense for an investigator banking a valuable sample set to join their resource with ours."

Clinical data on samples would go directly to Boston

MAVERIC already houses an 8,000-square-feet genetic-tissue core laboratory, with 36 large electrical and liquid-nitrogen freezers, along with DNA extraction and analytical capacity. The core lab, directed by Dr. Mary Brophy, serves the Palo Alto-based DNA Bank of VA's CSP.

The new proposal will call for the MAVERIC facility to be the main national tissue repository, with 10 or so VA hospitals around the country serving as collection sites. Along with the actual specimens, all related patient data, such as lab values, would be collected in a standardized fashion and submitted directly to the central bank. That way, investigators in the future would not have to track down missing information critical to their study. The goal is a researcher-friendly system.

Many ethical concerns already addressed through Palo Alto project

What about the myriad scientific and ethical issues involved in collecting and storing human samples? The national biorepository would rely on many of the policies now being formulated by Palo Alto committees working with the CSP bank, under the directorship of Phi Lavori, PhD.

"We're still looking for the optimal way to do this, and we expect significant, useful dialogue to result from the process," said Rose.

But one thing is clear even now: With VA's resources, the agency's national tissue bank could rival any in academia or private industry for quality and scope.

"No other biorepository initiative in the country has the potential assets that VA has, in terms of the size of the patient population, the willingness of the patients to participate in clinical research, and the depth of the stored clinical data," said Fiore. "Many of the current repositories are commerical and are motivated by profit. Our initiative will be purely motivated by the science we will generate and the potential benefits that will feed back to veterans' health care."

For more information, contact David Rose at (617) 232-9500, ext. 6137, or david.rose@med.va.gov. ■

Career achievements

Richard L. Lieber, PhD, a Rehabilitation Research and Development career scientist in San Diego, received the Nicolas Andry Award for his contributions to orthopedic knowledge and practice. The $15,000 award, from the Association of Bone and Joint Surgeons and *Clinical Orthopaedics and Related Research,* will help support Lieber's work in developing a new approach to surgical reconstruction of the arm using laser diffraction.

Robert L. Ruff, MD, PhD, associate director of VA's Center for Functional Electrical Stimulation in Cleveland, was named 2002 Doctor of the Year by the Myasthenia Gravis Foundation (MGF). Ruff, who has served on MGF's board of directors and medical/scientific advisory board, was cited for his efforts in research, patient education, fund raising and other areas. "Dr. Ruff is a wonderful mixture of doctor, educator, and compassionate human being," said the foundation's chief executive officer, Debora Boelz.

Pioneer in fighting brain tumors wins major grant

Edward A. Neuwelt, MD, a neurosurgeon with the Portland VA Medical Center and director of the Blood-Brain Barrier Program at Oregon Health and Science University (OHSU), received a $3.7 million Javits Neuroscience Investigator Award from the National Institute of Neurological Disorders and Stroke. Neuwelt will continue his pioneering research on a unique method of delivering chemotherapy to the brain by temporarily disrupting the blood-brain barrier.

In the early 1980s Neuwelt discovered a way to "outsmart" the blood-brain barrier, which protects the brain from pathogens and other foreign molecules in the bloodstream. His method uses a concentrated sugar solution to temporarily shrink the tightly knit endothelial cells that form the barrier, thus widening the gaps between the cells. Chemotherapy drugs can then to be administered directly to the site of a brain tumor through a catheter in a neck artery. The method delivers up to 100 times more drug to the tumor and its surrounding area than standard chemotherapy.

The Blood-Brain Barrier Program has treated some 500 patients using the disruption procedure. Each year, about 12,000 Americans die from brain tumors.

The Javits Investigator Awards are named for the late U.S. Senator Jacob Javits, who lived with Lou Gehrig's disease for many years and was a strong advocate for neurological research. ■

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fact, the placebo patients reported even better scores than the debridement patients at certain points during the follow-up. Throughout the two years, the patients remained unaware of whether they had received real or mock surgery. ■

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